

## Review Article

### Melioidosis

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#### Abstract:

*Melioidosis is an important disease caused by a Gram-negative bacterium, Burkholderia pseudomallei. The true incidence of melioidosis is unknown for most countries of the world including Bangladesh. Due to its increasing incidence in many countries of the world it is an important issue now days. Due to variability of clinical features and limited availability of laboratory facilities the disease remains largely under-reported. Early and specific diagnosis is important to ensure a favourable outcome regarding this disease. In this paper history, transmission, sign symptoms, diagnosis and prevention of melioidosis are critically reviewed to know about something regarding this disease*

**Key words:** Melioidosis, Burkholderia pseudomallei, Biological warfare.

#### Introduction

Melioidosis is an infectious disease caused by a Gram-negative bacterium, Burkholderia pseudomallei, found in soil and water. It is also called Whitmore's disease. It is of public health importance in endemic areas, particularly in Thailand and northern Australia. It exists in acute and chronic forms. Symptoms may include pain in chest, bones, or joints; cough; skin infections, lung nodules and pneumonia<sup>1</sup>.

#### Epidemiology

Melioidosis is endemic in parts of Southeast Asia (including Thailand, Laos and southern China, Singapore, Malaysia, Burma and Vietnam), Taiwan, and northern Australia<sup>2</sup>. Multiple cases have also been

described in Hong Kong and Brunei India, and sporadic cases in Central and South America, the Middle East, the Pacific and several African countries. Although only one case of Melioidosis has ever been reported in Bangladesh<sup>3</sup>, at least five cases have been imported to the UK from that country, which suggests that Melioidosis is endemic to that country and that there is a serious problem of underdiagnosis or under-reporting, most likely due to a lack of adequate laboratory facilities.

Melioidosis is a recognised disease in animals, including cats, goats, sheep, and horses. Cattle, water buffalo, and crocodiles are considered to be relatively resistant to Melioidosis despite their constant exposure to mud<sup>4</sup>. Burkholderia pseudomallei is normally found

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in soil and surface water. A history of contact with soil or surface water is therefore almost invariable in patients with Melioidosis<sup>5</sup>. The single most important risk factor for developing severe Melioidosis is diabetes mellitus. Other risk factors include thalassaemia, kidney disease, occupation (rice paddy farmers), and cystic fibrosis. The mode of infection is believed to be either through a break in the skin, or through the inhalation of aerosolized *B. pseudomallei*. Person-to-person spread has been described but is extremely unusual<sup>6</sup>.

### **Clinical features acute melioidosis**

The mean incubation period of acute melioidosis is 9 days (range 1-21 days)<sup>7</sup>. Patients with latent melioidosis may be symptom free for decades; the longest period between presumed exposure and clinical presentation is 62 years. A patient with active melioidosis usually presents with fever. Pain or other symptoms may be suggestive of a clinical focus, which is found in around 75% of patients. Such symptoms include cough or pleuritic chest pain suggestive of pneumonia, bone or joint pain suggestive of osteomyelitis or septic arthritis, or cellulitis. Intra-abdominal infection (including liver and/or splenic abscesses, or prostatic abscesses) do not usually present with focal pain. Imaging of these organs using ultrasound or CT should be performed routinely<sup>8</sup>. Up to 25% of patients, no focus of infection is found and the diagnosis is usually made on blood cultures or throat swab. Melioidosis is said to be able to affect any organ in the body except the heart valves (endocarditis). Less common manifestations include intravascular infection, lymph node abscesses (1.2-2.2%), myocarditis, mediastinal infection, and thyroid and scrotal abscesses and ocular infection<sup>9</sup>.

### **Chronic melioidosis**

Chronic melioidosis is usually defined by a duration of symptoms greater than 2 months and occurs in approximately 10% of patients. The clinical presentation includes chronic skin infection, skin ulcers and lung nodules or chronic pneumonia, closely mimicking tuberculosis, sometimes being called "Vietnamese tuberculosis". Chronic melioidosis can mimic tuberculous pericarditis, myocarditis, mediastinal infection, and thyroid and scrotal abscesses and ocular infection<sup>10</sup>.

### **Diagnosis**

A definitive diagnosis is made by culturing the organism from any clinical sample, because the organism is never

part of the normal human flora. A complete screen (blood culture, sputum culture, urine culture, throat swab and culture of any aspirated pus) should be performed on all patients with suspected melioidosis. A definitive diagnosis is made by growing *B. pseudomallei* from any site. A throat swab is not sensitive but is 100% specific if positive, and compares favourably with sputum culture<sup>11</sup>.

The sensitivity of urine culture is increased if a centrifuged specimen is cultured, and any bacterial growth should be reported (not just growth above 10<sup>4</sup> organisms/ml which is the usual cut off). Very occasionally, bone marrow culture may be positive in patients who have negative blood cultures for *B. pseudomallei*, but these are not usually recommended. There is also a serological test for melioidosis (indirect haemagglutination), but this is not commercially available in most countries. A specific direct immunofluorescent test and latex agglutination, based on monoclonal antibodies, are used widely in Thailand but are not available elsewhere<sup>12</sup>.

### **Treatment**

The treatment of melioidosis divided into two stages. An intravenous high intensity phase and An eradication phase to prevent recurrence.

#### **Intravenous intensive phase**

Intravenous ceftazidime is the current drug of choice for treatment of acute melioidosis. Meropenem, imipenem and cefoperazone-sulbactam (Sulperazone) are also active. Intravenous amoxicillin-clavulanate (co-amoxiclav) may be used if none of the above four drugs are available. Intravenous antibiotics are given for a minimum of 10 to 14 days, and are not usually stopped until the patient's temperature has returned to normal for more than 48 hours. The median fever clearance time in melioidosis is 10 days and failure of the fever to clear is not a reason to alter treatment. It is not uncommon for patients to require parenteral treatment continuously for a month or more<sup>13</sup>.

#### **Eradication phase**

Following the treatment of the acute disease, it is recommended that eradication treatment with co-trimoxazole and doxycycline be used for 12 to 20 weeks to reduce the rate of recurrence. Co-amoxiclav is an alternative for those patients who are unable to take co-trimoxazole and<sup>14</sup>.

## Surgical treatment

Surgical drainage is usually indicated for prostatic abscesses, septic arthritis and parotid abscesses. But it is not usually indicated for hepatosplenic abscesses<sup>15</sup>.

## Prognosis

Without access to appropriate antibiotics (principally ceftazidime or meropenem), the septicemic form of melioidosis has a mortality rate that exceeds 90%. With appropriate antibiotics, the mortality rate is about 10% for uncomplicated cases but up to 80% for cases with bacteraemia or severe sepsis. Recurrence occurs in 10 to 20% of patients<sup>16</sup>.

## Prevention

Person-to-person transmission is exceedingly unusual and patients with melioidosis should not be considered contagious. Lab workers should handle *Burkholderia pseudomallei* under BSL-3 isolation conditions, as laboratory acquired melioidosis has been described.

In endemic areas, people (rice-paddy farmers in particular) are warned to avoid contact with soil, mud and surface water where possible<sup>17</sup>.

## Post-exposure prophylaxis

After exposure to *B. pseudomallei* (particularly following a laboratory accident) combined treatment with co-trimoxazole and doxycycline is recommended. Trovafloxacin and grepafloxacin have been shown to be effective in animal models<sup>18</sup>.

## Vaccination

There are no vaccines currently licensed for the prevention of melioidosis

## Biological warfare potential

The agent has the potential to be developed as a biological weapon. It is classed by the US Centers for Disease Control (CDC) as a Category B agent. *B. pseudomallei*, like its relative *B. mallei* which causes Glanders, was studied by the U.S. as a potential biological warfare agent, but was never weaponized. It has been reported that the Soviet Union was also experimenting with *B. pseudomallei* as a biological warfare agent<sup>19</sup>.

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